

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Tibotec Pharmaceuticals Ltd.

Serial No.: Art Unit:

Filed : Examiner:

For : PROCESS FOR THE PREPARATION OF (3R,3AS,6AR)-HEXAHYDROFURO [2,3-B] FURAN-3-YL (1S,2R)-3-[[ (4-AMINOPHENYL) SULFONYL] (ISOBUTYL) AMINO]-1-BENZYL-2-HYDROXYPROPYLCARBAMATE

Commissioner for Patents  
Washington, D.C. 20231

CERTIFICATE UNDER 37 CFR 3.73(b)

Tibotec Pharmaceuticals Ltd., a Corporation, certifies that it is the assignee of the entire right, title and interest in the patent application identified above by virtue of either:

- A.  An assignment from the inventor(s) of the patent application identified above. The assignments were recorded in the Patent and Trademark Office at Reel , Frame , or for which a copy thereof is attached.

OR

- B.  A chain of title from the inventor(s), or the patent application identified above, to the current assignee as shown below:

1. From:  
To:  
The document was recorded in the Patent and Trademark Office at Reel , Frame , or for which a copy thereof is attached.
2. From:  
To:  
The document was recorded in the Patent and Trademark Office at Reel , Frame , or for which a copy thereof is attached.
3. From:

To:

The document was recorded in the Patent and Trademark Office at Reel , Frame , or for which a copy thereof is attached.

Additional documents in the chain of title are listed on a supplemental sheet.

Copies of assignments or other documents in the chain of title are attached.

The undersigned has reviewed all the documents in the chain of title of the patent application identified above and, to the best of undersigned's knowledge and belief, title is in the assignee identified above.

The undersigned (whose title is supplied below) is empowered to sign this certificate on behalf of the assignee.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements, and the like so made, are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

7 April 2006  
Date

  
Signature

Frank Daeleman  
Typed or Printed Name

Proxy Holder  
Title

A S S I G N M E N T

Serial No.  
Filed

WHEREAS, Nicolaas Martha Felix GOYVAERTS, residing at Welvaartstraat 69, B-2590 Berlaar, Belgium (hereinafter called "Assignor") has made jointly with Piet Tom Bert Paul WIGERINCK, residing at Kardinaal Cardijnstraat 29, B-2840 Terhagen, Belgium; Hartmut Burghard ZINSER, residing at J.J. Wepferstrasse 5, CH-8200 Schaffhausen, Switzerland and Birgit M. EBERT, residing at Hochstrasse 311, CH-8200 Schaffhausen, Switzerland certain new and useful inventions or discoveries relating to

PROCESS FOR THE PREPARATION OF (3R,3AS,6AR)-HEXAHYDROFURO [2,3-B]  
FURAN-3-YL (1S,2R)-3-[[[4-AMINOPHENYL) SULFONYL] (ISOBUTYL) AMINO]-1-  
BENZYL-2-HYDROXYPROPYLCARBAMATE

for which he has on the day of , 2005  
executed an application for Letters Patent of the United States;  
(Applicant(s) hereby authorize the legal representative(s) of  
record to enter herein the supplemental identification  
information for this application as provided by the US PTO); and

WHEREAS, TIBOTEC BVBA, a corporation of the State of  
Belgium, (hereinafter called "Assignee"), is desirous of  
acquiring Assignor's entire right, title, and interest therein:

NOW, THEREFORE, BE IT KNOWN that for and in  
consideration of the sum of One Dollar and other valuable  
considerations to them moving, the receipt of which is hereby  
acknowledged, Assignor has sold, assigned, and transferred, and  
does hereby sell, assign and transfer unto said Assignee his  
entire right, title and interest in and to all said inventions  
and discoveries disclosed in said application whose  
identification above by serial number and filing date, when  
available is hereby authorized, and in and to said application,  
all substitutions, divisions, and continuations thereof, and in  
and to all Letters Patent, United States and foreign, that may  
be granted for said inventions and discoveries, and in and to  
all extensions, renewals, and reissues thereof, the same to be  
held and enjoyed by said Assignee, its successors and assigns,  
as fully and entirely as the same would have been held and  
enjoyed by Assignor if this Assignment and sale had not been  
made;

And Assignor hereby authorizes and requests the Commissioner of Patents of the United States to issue said Letters Patent in accordance with this Assignment;

And for the consideration aforesaid, Assignor covenants and agrees with said Assignee that he has a full and unencumbered title to the inventions and discoveries above described and hereby assigned, which title they warrant unto said Assignee, its successors and assigns;

And for the consideration aforesaid, Assignor further covenants and agrees that he will, whenever requested, but without cost to him promptly communicate to said Assignee or its representatives any facts known to them relating to said inventions and discoveries, testify in any interference or legal proceedings involving said inventions and discoveries, and execute any additional papers that may be necessary to enable said Assignee or its representatives, successors, nominees, or assigns to secure full and complete protection for the said inventions and discoveries or that may be necessary to vest in said Assignee the complete title to the said inventions and discoveries and patents hereby conveyed and to enable it to record said title.

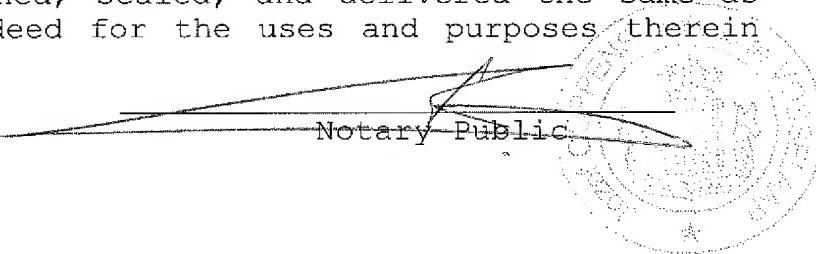
IN TESTIMONY WHEREOF, Assignor has hereunto set his hand and seal this 13 day of January , 2005

  
\_\_\_\_\_  
(L.S.)  
Nicolaas M.F. Goyvaerts

STATE OF )  
              )  
              ) ss.  
COUNTY OF )

BE IT REMEMBERED, That on this 26<sup>th</sup> day of January 2005 , before me, a Notary Public, personally appeared

who I am satisfied are the persons named in and who executed the foregoing instrument in my presence, and I having first made known to him the contents thereof, they did acknowledge that he signed, sealed, and delivered the same as his voluntary act and deed for the uses and purposes therein expressed.

  
Notary Public

A S S I G N M E N T

Serial No.

Filed

WHEREAS, Piet Tom Bert Paul WIGERINCK, residing at Kardinaal Cardijnstraat 29, B-2840 Terhagen, Belgium (hereinafter called "Assignor") has made jointly with Nicolaas Martha Felix GOYVAERTS, residing at Welvaartstraat 69, B-2590 Berlaar, Belgium; Hartmut Burghard ZINSER, residing at J.J. Wepferstrasse 5, CH-8200 Schaffhausen, Switzerland and Birgit M. EBERT, residing at Hochstrasse 311, CH-8200 Schaffhausen, Switzerland certain new and useful inventions or discoveries relating to

**PROCESS FOR THE PREPARATION OF (3R,3AS,6AR)-HEXAHYDROFURO [2,3-B] FURAN-3-YL (1S,2R)-3-[[[4-AMINOPHENYL) SULFONYL] (ISOBUTYL) AMINO]-1-BENZYL-2-HYDROXYPROPYLCARBAMATE**

for which he has on the day of , 2005 executed an application for Letters Patent of the United States; (Applicant(s) hereby authorize the legal representative(s) of record to enter herein the supplemental identification information for this application as provided by the US PTO); and

WHEREAS, TIBOTEC BVBA, a corporation of the State of Belgium, (hereinafter called "Assignee"), is desirous of acquiring Assignor's entire right, title, and interest therein:

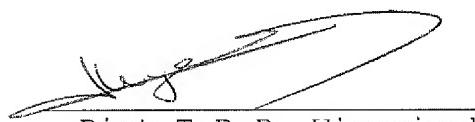
NOW, THEREFORE, BE IT KNOWN that for and in consideration of the sum of One Dollar and other valuable considerations to them moving, the receipt of which is hereby acknowledged, Assignor has sold, assigned, and transferred, and does hereby sell, assign and transfer unto said Assignee his entire right, title and interest in and to all said inventions and discoveries disclosed in said application whose identification above by serial number and filing date, when available is hereby authorized, and in and to said application, all substitutions, divisions, and continuations thereof, and in and to all Letters Patent, United States and foreign, that may be granted for said inventions and discoveries, and in and to all extensions, renewals, and reissues thereof, the same to be held and enjoyed by said Assignee, its successors and assigns, as fully and entirely as the same would have been held and enjoyed by Assignor if this Assignment and sale had not been made;

And Assignor hereby authorizes and requests the Commissioner of Patents of the United States to issue said Letters Patent in accordance with this Assignment;

And for the consideration aforesaid, Assignor covenants and agrees with said Assignee that he has a full and unencumbered title to the inventions and discoveries above described and hereby assigned, which title they warrant unto said Assignee, its successors and assigns;

And for the consideration aforesaid, Assignor further covenants and agrees that he will, whenever requested, but without cost to him promptly communicate to said Assignee or its representatives any facts known to them relating to said inventions and discoveries, testify in any interference or legal proceedings involving said inventions and discoveries, and execute any additional papers that may be necessary to enable said Assignee or its representatives, successors, nominees, or assigns to secure full and complete protection for the said inventions and discoveries or that may be necessary to vest in said Assignee the complete title to the said inventions and discoveries and patents hereby conveyed and to enable it to record said title.

IN TESTIMONY WHEREOF, Assignor has hereunto set his hand and seal this 19<sup>th</sup> day of January , 2005

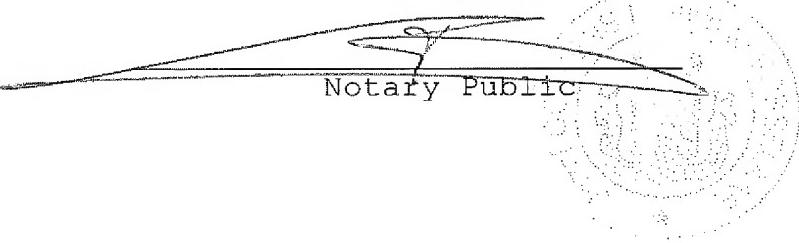


(L.S.)  
Piet T.B.P. Wigerinck

STATE OF )  
              )  
              ) ss.  
COUNTY OF )

BE IT REMEMBERED, That on this 24<sup>th</sup> day of January 2005 , before me, a Notary Public, personally appeared

who I am satisfied are the persons named in and who executed the foregoing instrument in my presence, and I having first made known to him the contents thereof, they did acknowledge that he signed, sealed, and delivered the same as his voluntary act and deed for the uses and purposes therein expressed.



Notary Public

A S S I G N M E N T

Serial No.

Filed

WHEREAS, Hartmut Burghard ZINSER, residing at J.J. Wepferstrasse 5, CH-8200 Schaffhausen, Switzerland and Birgit M. EBERT, residing at Hochstrasse 311, CH-8200 Schaffhausen, Switzerland (hereinafter called "Assignors") have made jointly with Nicolaas Martha Felix GOYVAERTS, residing at Welvaartstraat 69, B-2590 Berlaar, Belgium and Piet Tom Bert Paul WIGERINCK, residing at Kardinaal Cardijnstraat 29, B-2840 Terhagen, Belgium certain new and useful inventions or discoveries relating to

PROCESS FOR THE PREPARATION OF (3R,3AS,6AR)-HEXAHYDROFURO [2,3-B]  
FURAN-3-YL (1S,2R)-3-[(4-AMINOPHENYL) SULFONYL] (ISOBUTYL) AMINO]-1-  
BENZYL-2-HYDROXYPROPYLCARBAMATE

for which they have on the              day of              , 2005  
executed an application for Letters Patent of the United States;  
(Applicant(s) hereby authorize the legal representative(s) of  
record to enter herein the supplemental identification  
information for this application as provided by the US PTO); and

WHEREAS, CILAG AG, a corporation of the State of  
Switzerland, (hereinafter called "Assignee"), is desirous of  
acquiring Assignors' entire right, title, and interest therein:

NOW, THEREFORE, BE IT KNOWN that for and in  
consideration of the sum of One Dollar and other valuable  
considerations to them moving, the receipt of which is hereby  
acknowledged, Assignors have sold, assigned, and transferred,  
and do hereby sell, assign and transfer unto said Assignee their  
entire right, title and interest in and to all said inventions  
and discoveries disclosed in said application whose  
identification above by serial number and filing date, when  
available is hereby authorized, and in and to said application,  
all substitutions, divisions, and continuations thereof, and in  
and to all Letters Patent, United States and foreign, that may  
be granted for said inventions and discoveries, and in and to  
all extensions, renewals, and reissues thereof, the same to be  
held and enjoyed by said Assignee, its successors and assigns,  
as fully and entirely as the same would have been held and  
enjoyed by Assignors if this Assignment and sale had not been  
made;

And Assignors hereby authorize and request the Commissioner of Patents of the United States to issue said Letters Patent in accordance with this Assignment;

And for the consideration aforesaid, Assignors covenant and agree with said Assignee that he has a full and unencumbered title to the inventions and discoveries above described and hereby assigned, which title they warrant unto said Assignee, its successors and assigns;

And for the consideration aforesaid, Assignors further covenant and agree that they will, whenever requested, but without cost to them promptly communicate to said Assignee or its representatives any facts known to them relating to said inventions and discoveries, testify in any interference or legal proceedings involving said inventions and discoveries, and execute any additional papers that may be necessary to enable said Assignee or its representatives, successors, nominees, or assign to secure full and complete protection for the said inventions and discoveries or that may be necessary to vest in said Assignee the complete title to the said inventions and discoveries and patents hereby conveyed and to enable it to record said title.

IN TESTIMONY WHEREOF, Assignors have hereunto set their hand and seal this 17<sup>th</sup> day of March , 2005

Hartmut Zinsen (L.S.)  
Hartmut B. ZINSER

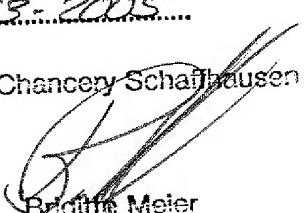
Birgit Ebert  
Birgit M. EBERT

STATE OF )  
            ) ss.  
COUNTY OF )

(L.S.) Schaffhausen, 17.03.2005



Town Chancery Schaffhausen

  
Brigitte Meier

### Legalization

Seen for legalization of the signature  
of Mr. Hartmut B. Zinsen and  
Mrs. Birgit M. Ebert  
..... 17.03.2005 .....

BE IT REMEMBERED, That on this        day of        ,  
200    , before me, a Notary Public, personally appeared

            who I am satisfied are the persons named in  
and who executed the foregoing instrument in my presence, and I  
having first made known to him the contents thereof, they did  
acknowledge that he signed, sealed, and delivered the same as  
his voluntary act and deed for the uses and purposes therein  
expressed.

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Notary Public

### General Assignment

WHEREAS, CILAG AG, having its place of business at Hochstrasse 201, CH-8205 Schaffhausen, Switzerland (hereinafter called "Assignor"), is the owner of certain new and useful inventions relating to

PROCESS FOR THE PREPARATION OF (3R,3AS,6AR)-HEXAHYDROFURO [2,3-B] FURAN-3-YL (1S,2R)-3-[[[4-AMINOPHENYL) SULFONYL] (ISOBUTYL) AMINO]-1-BENZYL-2-HYDROXYPROPYLCARBAMATE

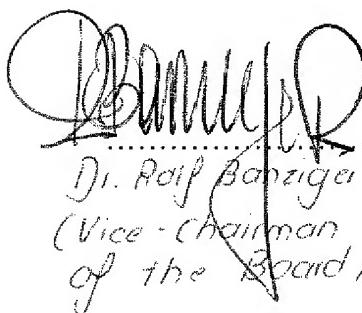
for which on the 23<sup>rd</sup> day of December 2003, European Patent Application no. 03104949.7 was filed at the European Patent Office and for which a US provisional application no. 60/568183 was filed on the 4<sup>th</sup> day of May 2004 at the USPTO.

WHEREAS, TIBOTEC PHARMACEUTICALS LTD., having its place of business at Little Island, Co Cork, Ireland (hereinafter called "Assignee") is desirous of acquiring Assignors' entire right, title and interest therein, including the right to claim priority thereof,

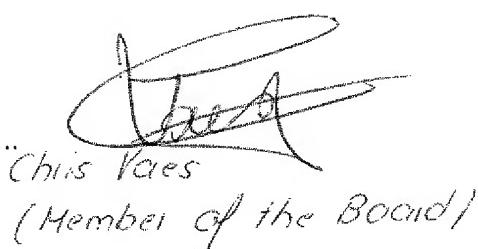
NOW, THEREFORE, BE IT KNOWN, that in view of good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Assignor hereby assigns and transfers, for all countries in the world, to said Assignee its entire right, title and interest, including the right to claim priority, in and to all said inventions disclosed in said applications and in and to said applications, and all foreign equivalents thereof, including all substitutions, divisions, and continuations thereof, and in and to all Letters Patent, that may be granted for said inventions, and in and to all extensions, renewals, and reissues thereof, the same to be held and enjoyed by said Assignee, its successors and assigns, as fully and entirely as the same would have been held and enjoyed by Assignor if this Assignment had not been made.

IN TESTIMONY WHEREOF, Assignor have hereunto set their hands and seals this  
7<sup>th</sup> day of April, 2005.

For CILAG AG



Dr. Rolf Banziger  
(Vice-Chairman  
of the Board)



Chris Vaes  
(Member of the Board)

## General Assignment

WHEREAS, TIBOTEC BVBA, having its place of business at Generaal De Wittelaan L11B3, B-2800 Mechelen, Belgium (hereinafter called "Assignor"), is the owner of certain new and useful inventions relating to

PROCESS FOR THE PREPARATION OF (3R,3AS,6AR)-HEXAHYDROFURO [2,3-B] FURAN-3-YL (1S,2R)-3-[[[4-AMINOPHENYL) SULFONYL] (ISOBUTYL) AMINO]-1-BENZYL-2-HYDROXYPROPYLCARBAMATE

for which on the 23<sup>rd</sup> day of December 2003, European Patent Application no. 03104949.7 was filed at the European Patent Office and for which a US provisional application no. 60/568183 was filed on the 4<sup>th</sup> day of May 2004 at the USPTO.

WHEREAS, TIBOTEC PHARMACEUTICALS LTD., having its place of business at Little Island, Co Cork, Ireland (hereinafter called "Assignee") is desirous of acquiring Assignors' entire right, title and interest therein, including the right to claim priority thereof,

NOW, THEREFORE, BE IT KNOWN, that in view of good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Assignor hereby assigns and transfers, for all countries in the world, to said Assignee its entire right, title and interest, including the right to claim priority, in and to all said inventions disclosed in said applications and in and to said applications, and all foreign equivalents thereof, including all substitutions, divisions, and continuations thereof, and in and to all Letters Patent, that may be granted for said inventions, and in and to all extensions, renewals, and reissues thereof, the same to be held and enjoyed by said Assignee, its successors and assigns, as fully and entirely as the same would have been held and enjoyed by Assignor if this Assignment had not been made.

IN TESTIMONY WHEREOF, Assignor have hereunto set their hands and seals this  
27<sup>th</sup> day of January , 2005.

For Tibotec BVBA

Paul Stoffels

